

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L12	21	LEVENTER adj STEVEn	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:35
L13	51	HARRIS adj HERBERT	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:35
L14	41	KUCHARIK adj 'ROBERT	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:36
L15	41	KUCHARIK adj ROBERT	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:36
L16	76	l12 l13 l14	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:36
L18	21	l16 and 2,3-benzodiazepines	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:40
L19	6125	xia.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:40
L20	1	l19 and 2,3-benzodiazepines	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:45

## EAST Search History

L21	2	"5492907".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 17:45
L22	28	l16 and benzodiazepine	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 18:47
L23	0	tofosipam	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 18:48
L24	178	tofisopam	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 18:48
L25	13	l24 same metabolite\$	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/12/12 18:48
L26	16	("3736315"   "4322346"   "4423044"   "4614740"   "4835152"   "4840948"   "5204343"   "5288863"   "5459137"   "5519019"   "5521174"   "5639751"   "5891871"   "6075018"   "6080736").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 20:01
L27	9175	l26 and 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8- dimethoxy-5H-2,3 -benzodiazepine	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 19:54
L28	770	l26 and 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8- dimethoxy-5H-2,3-benzodiazepine	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 19:54
L29	2	l26 and dimethoxy-5H-2,3-benzodiazepine	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 19:57
L30	2	l26 and hydroxy and methoxyphenyl	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 19:57
L31	12	l26 and compound.clm.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 20:01
L32	5	l26 and compounds.clm.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 20:01
L33	13	l26 and formula.clm.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 20:01

## EAST Search History

L34	0	I26 and formulae.clm.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 20:01
L35	13	I31 I32 I33	US-PGPUB; USPAT; USOCR	OR	OFF	2007/12/12 20:02

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NEWS 4 JUL 02 CHEMCATS accession numbers revised  
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NEWS 6 JUL 16 Capplus enhanced with French and German abstracts  
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NEWS 24 OCT 19 BEILSTEIN updated with new compounds  
NEWS 25 NOV 15 Derwent Indian patent publication number format enhanced  
NEWS 26 NOV 19 WPIX enhanced with XML display format  
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CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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\* \* \* \* \*

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The normal schedule for STN maintenance downtime (22:00 to 01:00) will resume on December 22.

\*\*\*\*\*

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=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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=> s 730962-81-9

L1 1 730962-81-9  
(730962-81-9/RN)

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN

RN 730962-81-9 REGISTRY

ED Entered STN: 23 Aug 2004

CN Phenol, 5-[(5S)-5-ethyl-7,8-dimethoxy-4-methyl-5H-2,3-benzodiazepin-1-yl]-2-methoxy- (CA INDEX NAME)

OTHER NAMES:

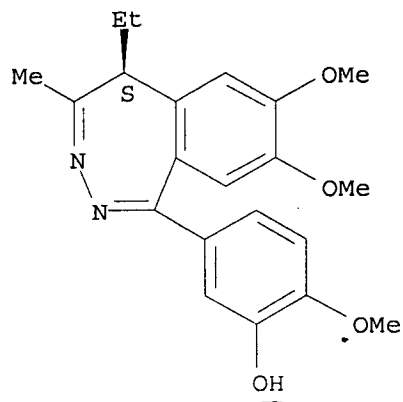
CN (S)-1-(3-Hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine

FS STEREOSEARCH

MF C21 H24 N2 O4

SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

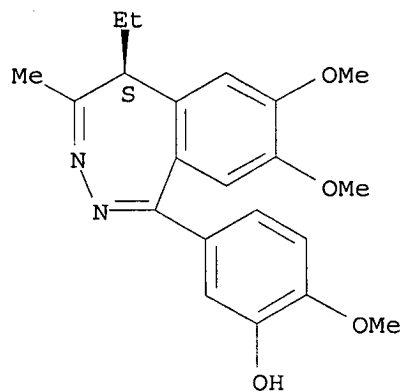
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L2 0 730962-81-9/CN

=> s 730962-81-9/rn  
L3 1 730962-81-9/RN

=> d l3

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 730962-81-9 REGISTRY  
ED Entered STN: 23 Aug 2004  
CN Phenol, 5-[(5S)-5-ethyl-7,8-dimethoxy-4-methyl-5H-2,3-benzodiazepin-1-yl]-  
2-methoxy- (CA INDEX NAME)  
OTHER NAMES:  
CN (S)-1-(3-Hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-  
benzodiazepine  
FS STEREOSEARCH  
MF C21 H24 N2 O4  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FIL CAPLUS

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

9.30

9.51

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=> s l3

L4 3 L3

=> d l4 bib ab 1-3

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:1080692 CAPLUS

DN 142:56375

TI Modulation of dopamine responses with substituted (S)-2,3-benzodiazepines

IN Leventer, Steven M.; Harris, Herbert W.; Kucharik, Robert F.

PA USA

SO U.S. Pat. Appl. Publ., 33 pp.

CODEN: USXXCO

DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	US 2004254173	A1	20041216	US 2003-461290	20030613
PRAI	US 2003-461290		20030613		
OS	MARPAT 142:56375				

AB There is provided a method of modulating dopamine responses in the central nervous system of an individual or a method of treating a dopamine-mediated disorder in an individual not suffering from seizures or convulsions which comprises administering to the individual an effective amount of at least one compound of formula (I) [R1 = C1-7 hydrocarbyl or C2-6 heteroalkyl; R2 = H, C1-7 hydrocarbyl; wherein R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; R3, R4, R5, R6 = OH, C1-7 hydrocarbyl, CF3, C1-7 hydrocarbyloxy, acyloxy, NH2, -NH(C1-6alkyl), -N(C1-6 alkyl)2, -NH-acyl, halogen; wherein R5 and R6 may combine to form a 5-, 6- or 7-membered heterocyclic ring] or pharmaceutically acceptable salts thereof or said compound comprising an (S)-enantiomer substantially free of the (R)-enantiomer of the same compound. The above dopamine-mediated disorder comprises a neurol. disorder or a neuropsychiatric disorder. The neurol. disorder includes Huntington's chorea, Parkinson's disease, periodic limb movement syndrome, restless leg syndrome, hyperkinesias, Tourette's syndrome, Pick's disease, punch drunk syndrome, progressive subnuclear palsy, multiple systems atrophy, Landau-Kleffner syndrome, benign essential blepharospasm, amyotrophic lateral sclerosis, medication-induced movement disorders, and cognitive disorders. The neuropsychiatric disorder includes psychosis, personality disorders, psychiatric mood disorders, conduct and impulse disorders, schizophrenia, bipolar disorders, dysphoric mania, anxiety disorders, depression, panic disorders, agoraphobia, obsessive-compulsive disorders and eating disorders. Thus, 4.41 g (10 mmol) 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrilium chloride hydrochloride was dissolved in methanol (35 mL) at a temperature of 40°. After cooling to 20-25°, hydrazine hydrate (0.75 g, 15 mmol, dissolved in 5 mL methanol) was added and the resulting mixture was allowed to react while monitoring the reaction by HPLC and when complete, was evaporated to dryness. The residue was triturated with cold water (3 mL), filtered and dried to yield the crude 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine (racemic tofisopam) which was subsequently triturated with hot EtOAc to yield the pure product. Racemic tofisopam was resolved by a Chirobiotic V column (ASTEAC, Whippany, N.J.) to give (R)-tofisopam and (S)-tofisopam. (R)-tofisopam did not affect apomorphine-induced hypothermia in mice. Racemic tofisopam at 64 mg/kg tended to behave as a weak dopamine antagonist, i.e., lowering the rectal temperature at the thirty and sixty minute time points. However this trend was not statistically significant. (S)-tofisopam behaved as a weak dopamine antagonist at the 16 mg/kg dose at sixty minutes after apomorphine administration, i.e., showing a slight but statistically significant elevation in temperature. At the higher doses, (S)-tofisopam demonstrated dopamine antagonism at both the thirty minute and sixty minute time points, i.e., lowering the rectal temperature at both time points.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2004:995773 CAPLUS  
DN 141:410971  
TI A preparation of 2,3-benzodiazepine derivatives, useful as antipyretic agents  
IN Harris, Herbert W.; Kucharik, Robert F.  
PA Vela Pharmaceuticals, Inc., USA  
SO U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 369,823.  
CODEN: USXXCO  
DT Patent  
LA English



FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004229866	A1	20041118	US 2004-781422	20040217
	US 2004162284	A1	20040819	US 2003-369823	20030219
	US 2004224943	A1	20041111	US 2004-827839	20040419
PRAI	US 2003-369823	A2	20030219		
	US 2004-781422	A2	20040217		

OS MARPAT 141:410971

AB The invention relates to a preparation of 2,3-benzodiazepine derivs. of formula I [wherein: R1 is hydrocarbyl or heteroalkyl; R2 is H or hydrocarbyl; R1 and R2 may combine to form a (carbo/hetero)cyclic ring; R3 and R4 are independently selected from OH, SH, NO2, halogen, or S-alkyl, etc.; R5 is substituted phenyl], useful as antipyretic agents. For instance, (S)-2,3-benzodiazepine derivative II was prepared via heterocyclization of diketone III with hydrazine and subsequent resolution. The prepared title compds. were tested in stress-induced hypothermia assay. (S)-enantiomer of tofisopam showed higher activity than the racemate or the (R)-enantiomer [dose: 64 mg/kg, (S)-tofisopam: 33 °C, (R)-tofisopam: 35.25 °C, racemate: 33.75 °C].

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:633284 CAPLUS

DN 141:162379

TI Pharmaceutical composition of 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine and uses thereof

IN Harris, Herbert W.; Leventer, Steven M.; Kucharik, Robert F.

PA Vela Pharmaceuticals, Inc., USA

SO U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004152695	A1	20040805	US 2003-728179	20031203
	CA 2510275	A1	20040819	CA 2003-2510275	20031203
	WO 2004069155	A2	20040819	WO 2003-US38641	20031203
	WO 2004069155	A3	20060112		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003303312	A1	20040830	AU 2003-303312	20031203
	EP 1575521	A2	20050921	EP 2003-815301	20031203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006514084	T	20060427	JP 2004-568017	20031203
	MX 2005PA05893	A	20060208	MX 2005-PA5893	20050602
PRAI	US 2002-430770P	P	20021203		
	WO 2003-US38641	W	20031203		

AB Pharmaceutical compns. comprise 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine, or a pharmaceutically acceptable salt thereof. The compns. are used for treating, preventing or delaying the onset of disorders mediated by LTB4 or TXA2.

=> file medicine

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=> s 13

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L5 7 L3

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L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2004:1080692 CAPLUS  
DN 142:56375  
TI Modulation of dopamine responses with substituted (S)-2,3-benzodiazepines  
IN Leventer, Steven M.; Harris, Herbert W.; Kucharik, Robert F.  
PA USA  
SO U.S. Pat. Appl. Publ., 33 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004254173	A1	20041216	US 2003-461290	20030613
PRAI	US 2003-461290		20030613		
OS	MARPAT 142:56375				

AB There is provided a method of modulating dopamine responses in the central nervous system of an individual or a method of treating a dopamine-mediated disorder in an individual not suffering from seizures or convulsions which comprises administering to the individual an effective amount of at least one compound of formula (I) [R1 = C1-7 hydrocarbyl or C2-6 heteroalkyl; R2 = H, C1-7 hydrocarbyl; wherein R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; R3, R4, R5, R6 = OH, C1-7 hydrocarbyl, CF3, C1-7 hydrocarbyloxy, acyloxy, NH2, -NH(C1-6alkyl), -N(C1-6 alkyl)2, -NH-acyl, halogen; wherein R5 and R6 may combine to form a 5-, 6- or 7-membered heterocyclic ring] or pharmaceutically acceptable salts thereof or said compound comprising an (S)-enantiomer substantially free of the (R)-enantiomer of the same compound  
The above dopamine-mediated disorder comprises a neurol. disorder or a neuropsychiatric disorder. The neurol. disorder includes Huntington's chorea, Parkinson's disease, periodic limb movement syndrome, restless leg syndrome, hyperkinesias, Tourette's syndrome, Pick's disease, punch drunk syndrome, progressive subnuclear palsy, multiple systems atrophy, Landau-Kleffner syndrome, benign essential blepharospasm, amyotrophic

lateral sclerosis, medication-induced movement disorders, and cognitive disorders. The neuropsychiatric disorder includes psychosis, personality disorders, psychiatric mood disorders, conduct and impulse disorders, schizophrenia, bipolar disorders, dysphoric mania, anxiety disorders, depression, panic disorders, agoraphobia, obsessive-compulsive disorders and eating disorders. Thus, 4.41 g (10 mmol) 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrilium chloride hydrochloride was dissolved in methanol (35 mL) at a temperature of 40°. After cooling to 20-25°, hydrazine hydrate (0.75 g, 15 mmol, dissolved in 5 mL methanol) was added and the resulting mixture was allowed to react while monitoring the reaction by HPLC and when complete, was evaporated to dryness. The residue was triturated with cold water (3 mL), filtered and dried to yield the crude 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine (racemic tofisopam) which was subsequently triturated with hot EtOAc to yield the pure product. Racemic tofisopam was resolved by a Chirobiotic V column (ASTEAC, Whippany, N.J.) to give (R)-tofisopam and (S)-tofisopam. (R)-tofisopam did not affect apomorphine-induced hypothermia in mice. Racemic tofisopam at 64 mg/kg tended to behave as a weak dopamine antagonist, i.e., lowering the rectal temperature at the thirty and sixty minute time points. However this trend was not statistically significant. (S)-tofisopam behaved as a weak dopamine antagonist at the 16 mg/kg dose at sixty minutes after apomorphine administration, i.e., showing a slight but statistically significant elevation in temperature. At the higher doses, (S)-tofisopam demonstrated dopamine antagonism at both the thirty minute and sixty minute time points, i.e., lowering the rectal temperature at both time points.

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:995773 CAPLUS  
 DN 141:410971  
 TI A preparation of 2,3-benzodiazepine derivatives, useful as antipyretic agents  
 IN Harris, Herbert W.; Kucharik, Robert F.  
 PA Vela Pharmaceuticals, Inc., USA  
 SO U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 369,823.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004229866	A1	20041118	US 2004-781422	20040217
	US 2004162284	A1	20040819	US 2003-369823	20030219
	US 2004224943	A1	20041111	US 2004-827839	20040419
PRAI	US 2003-369823	A2	20030219		
	US 2004-781422	A2	20040217		

OS MARPAT 141:410971  
 AB The invention relates to a preparation of 2,3-benzodiazepine derivs. of formula I [wherein: R1 is hydrocarbyl or heteroalkyl; R2 is H or hydrocarbyl; R1 and R2 may combine to form a (carbo/hetero)cyclic ring; R3 and R4 are independently selected from OH, SH, NO2, halogen, or S-alkyl, etc.; R5 is substituted phenyl], useful as antipyretic agents. For instance, (S)-2,3-benzodiazepine derivative II was prepared via heterocyclization of diketone III with hydrazine and subsequent resolution. The prepared title compds. were tested in stress-induced hypothermia assay. (S)-enantiomer of tofisopam showed higher activity than the racemate or the (R)-enantiomer [dose: 64 mg/kg, (S)-tofisopam: 33 °C, (R)-tofisopam: 35.25 °C, racemate: 33.75 °C].

L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2004:633284 CAPLUS  
 DN 141:162379  
 TI Pharmaceutical composition of 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine and uses thereof  
 IN Harris, Herbert W.; Leventer, Steven M.; Kucharik, Robert F.

PA Vela Pharmaceuticals, Inc., USA  
SO U.S. Pat. Appl. Publ., 19 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004152695	A1	20040805	US 2003-728179	20031203
	CA 2510275	A1	20040819	CA 2003-2510275	20031203
	WO 2004069155	A2	20040819	WO 2003-US38641	20031203
	WO 2004069155	A3	20060112		
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	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003303312	A1	20040830	AU 2003-303312	20031203
	EP 1575521	A2	20050921	EP 2003-815301	20031203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006514084	T	20060427	JP 2004-568017	20031203
	MX 2005PA05893	A	20060208	MX 2005-PA5893	20050602
PRAI	US 2002-430770P	P	20021203		
	WO 2003-US38641	W	20031203		

AB Pharmaceutical compns. comprise 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine, or a pharmaceutically acceptable salt thereof. The compns. are used for treating, preventing or delaying the onset of disorders mediated by LTB4 or TXA2.

L5 ANSWER 4 OF 7 TOXCENTER COPYRIGHT 2007 ACS on STN  
AN 2004:187210 TOXCENTER  
CP Copyright 2007 ACS  
DN CA14110162379N

TI Pharmaceutical composition of 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine and uses thereof

AU Harris, Herbert W.; Leventer, Steven M.; Kucharik, Robert F.

CS ASSIGNEE: Vela Pharmaceuticals, Inc.

PI US 2004152695 A1 5 Aug 2004

SO (2004) U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO.

CY UNITED STATES

DT Patent

FS CAPLUS

OS CAPLUS 2004:633284

LA English

ED Entered STN: 24 Aug 2004

Last Updated on STN: 23 Jan 2007

AB Pharmaceutical compns. comprise 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine, or a pharmaceutically acceptable salt thereof. The compns. are used for treating, preventing or delaying the onset of disorders mediated by LTB4 or TXA2.

L5 ANSWER 5 OF 7 USPATFULL on STN

AN 2004:321518 USPATFULL

TI Modulation of dopamine responses with substituted (S)-2,3-benzodiazepines

IN Leventer, Steven M., Langhorne, PA, UNITED STATES

Harris, Herbert W., Merion, PA, UNITED STATES

Kucharik, Robert F., Glenmoore, PA, UNITED STATES

PI US 2004254173 A1 20041216  
AI US 2003-461290 A1 20030613 (10)  
DT Utility  
FS APPLICATION  
LREP DRINKER BIDDLE & REATH, ONE LOGAN SQUARE, 18TH AND CHERRY STREETS,  
PHILADELPHIA, PA, 19103-6996  
CLMN Number of Claims: 34  
ECL Exemplary Claim: 1  
DRWN 11 Drawing Page(s)  
LN.CNT 1608  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Compounds according to formula I: ##STR1##

wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5 and R.sup.6 are as defined herein, and wherein the compound comprises the (S)-enantiomer, administered for modulation of dopamine responses and treatment of dopamine-mediated disorders.

L5 ANSWER 6 OF 7 USPATFULL on STN  
AN 2004:292777 USPATFULL  
TI Method of lowering body temperature with (S)-2,3-benzodiazepines  
IN Harris, Herbert W., Merion, PA, UNITED STATES  
Kucharik, Robert F., Glenmoore, PA, UNITED STATES  
PA Vela Pharmaceuticals, Inc., Lawrenceville, NJ (U.S. corporation)  
PI US 2004229866 A1 20041118  
AI US 2004-781422 A1 20040217 (10)  
RLI Continuation-in-part of Ser. No. US 2003-369823, filed on 19 Feb 2003,  
PENDING  
DT Utility  
FS APPLICATION  
LREP DRINKER BIDDLE & REATH, ONE LOGAN SQUARE, 18TH AND CHERRY STREETS,  
PHILADELPHIA, PA, 19103-6996  
CLMN Number of Claims: 31  
ECL Exemplary Claim: 1  
DRWN 2 Drawing Page(s)  
LN.CNT 1692  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB ##STR1##

An (S)-2,3-benzodiazepine of Formula I, substantially isolated from the corresponding (R)-enantiomer thereof, is administered to lower the body temperature of an individual.

L5 ANSWER 7 OF 7 USPATFULL on STN  
AN 2004:197389 USPATFULL  
TI Pharmaceutical composition of 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine and uses thereof  
IN Harris, Herbert W., Merion, PA, UNITED STATES  
Leventer, Steven M., Langhorne, PA, UNITED STATES  
Kucharik, Robert F., Glenmoore, PA, UNITED STATES  
PA Vela Pharmaceuticals, Inc., Lawrenceville, NJ (U.S. corporation)  
PI US 2004152695 A1 20040805  
AI US 2003-728179 A1 20031203 (10)  
PRAI US 2002-430770P 20021203 (60)  
DT Utility  
FS APPLICATION  
LREP DRINKER BIDDLE & REATH, ONE LOGAN SQUARE, 18TH AND CHERRY STREETS,  
PHILADELPHIA, PA, 19103-6996  
CLMN Number of Claims: 40  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1559  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Pharmaceutical compositions comprise 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine, or a

pharmaceutically acceptable salt thereof. The compositions are used for treating, preventing or delaying the onset of disorders mediated by LTB.sub.4 or TXA.sub.2.

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... a **precursor** of the pharmacologically active compound. The metabolic pathway of 2,3-BZs has been extensively studied in different species. **Tofisopam** metabolites ...

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... At the other extreme is another desmethyldiazepam **precursor**, prazepam. It is slowly transformed into the active substance ... Triazolam Brotizolam **Tofisopam** ...

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M Zappalà, S Grasso, N Micale, S Polimeni, C De ... - Mini Rev Med Chem, 2001 - ingentaconnect.com

... 1, GYKI 52466 2, **Tofisopam** ... The required chiral **precursor** 25 was obtained with the highly effective biocatalytic reduction of 3-(3,4- methylene-dioxyphenyl) ...

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A CZ, FR DE DK EE ES FI, GB GR, B JM... - NEUROSCIENCE, 2002 - publications.european-patent-office.org

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M Rizzo - Journal of Chromatography B: Biomedical Sciences and ..., 2000 - Elsevier ... 38]. The use of dimethyl silicone stationary phase gave better separation of **Tofisopam metabolites** than the cyanoethyl phase [48]. ...

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DW Landry, DF Klein... - US Patent 6,080,736, 2000 - Google Patents

... binding of BDZs is not due simply to pharmacokinetic factors since brain levels of diazepam and its **metabolite** desmethyldiazepam were unmodified by **tofisopam**. ...

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[Factors influencing monoamine metabolites and tryptophan in patients with alcohol dependence - all 3 versions »](#)

CM Banki - Journal of Neural Transmission, 1981 - Springer

... 91 conditions known to alter **metabolite** levels from sources other than central amine ... patients in the first days of abstinence received only **tofisopam**--a minor ...

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A Bond, M Lader - European Journal of Clinical Pharmacology, 1982 - Springer

... is slowly absorbed and distributed to the brain or it is a pro-drug and is transformed to an active **metabolite**. In vitro studies showed that **tofisopam** did not ...

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[The so-called "interconversion" of stereoisomeric drugs: An attempt at clarification - all 3 versions »](#)

B Testa, PA Carrupt, J Gal - Chirality, 1993 - doi.wiley.com

... **Tofisopam** thus offers an interesting and pharmacologically relevant example of ... stereose-

lectivity while the hydrogenation of the ketone **metabolite** is product ...

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... 2.697 Adenosine 206.4 3.635 Caffeine **metabolite** 1 206.4 2.74 Imidazole 205.2 3.637 Atenolol 200.5 ... 3.052 Flucytosine 200.5 4.237 Tiapride **metabolite** 212.2 ...

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[Recent Advances in the Clinical Pharmacology of Benzodiazepines Part I: Pharmacokinetics](#)

BS MD, GPMDS Psychiatrist - HUMAN PSYCHOPHARMACOLOGY, 1987 - doi.wiley.com

... Parent drug Active **metabolite** Elimination half-live Reference (h) Meanor Range median Midazolam Triazolam Brotizolam **Tofisopam** Cinolazepam ...

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Absence of Liver DNA Fragmentation in Rats Treated with High Oral Doses of 32 Benzodiazepine Drugs - all 3 versions »

PIA CARLO, F RENATA, A LEDDA, G BRAMBILLA - Toxicological Sciences, 2001 - Soc Toxicology

... diazepam, flunitrazepam, flurazepam, medazepam, nitrazepam, and **tofisopam**) the dose ... these drugs are extensively transformed into **metabolites**, and because ...

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Tofizopam: a benzodiazepine derivative without sedative effect.

J Kanto, L Kangas, T Leppanen, M Mansikka, ML ... - Int J Clin Pharmacol Ther Toxicol, 1982 - ncbi.nlm.nih.gov

... to these results, the active component seems to be an unknown **metabolite** of tofizopam ...

Benzodiazepines; **tofisopam**. PMID: 6125483 [PubMed - indexed for MEDLINE]

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... prazepam; 15 = clobazam; 16 = **tofisopam**) were dissolved in methanol at a concentration of 1 mg/ml; 500 nl of ... (TDGA) to be the only CMC-**metabolite** detectable in ...

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